Date: August, 2015
Global Relations and Research Coordination Office RIKEN

Research Project Mid-term Evaluation Result

The following research project underwent a mid-term evaluation in accordance to Clause 10 and 11, Chapter 2 of the *Regulations for Research and Development Evaluations* (Regulation No. 74, October 1, 2003.)

Evaluation system:
Two experts from outside of RIKEN and three RIKEN Science Council Research Programs Committee members were appointed as reviewers for the following research project. The reviewers evaluated the project based on the reporting session held on June 11, 2015.

Reviewers list:
External experts (alphabetical order)
1) Teizo KITAGAWA, Professor, University of Hyogo
2) Gunji SAITO, Professor, Meijo University,

RIKEN Science Council Research Program committee member(alphabetical order)
3) Hideki HIRAYAMA, Chief Scientist, Quantum Optodevice Laborator
4) Zhaomin HOU, Chief Scientist, Organometallic Chemistry Laboratory
5) Toshihide KOBAYASHI, Chief Scientist, Lipid Biology Laboratory

Research project brief overview
Project name: Molecular Systems Research
Project Leader： Tahei TAHARA
Project duration： April, 2012～March, 2016（5 years）
Budget allocated：Total of 606,515 thousand Yen（3 years）
Research overview：
As materials become more complex, they contain more molecules or more molecular parts and start showing amazing functions that cannot be realized by a simple molecule. The study of the properties and functions of such complex molecular systems is critically important in materials science today. We gather researchers having high activities in chemistry, physics, biology and engineering, and carry out interdisciplinary research for elucidating, controlling and creating highly efficient molecular systems. This project consists of four teams: (1) Team for analyzing molecular systems, (2) Team for controlling molecular systems, (3) Team for biological molecular systems, and (4) Team for engineering molecular systems.

1. Comprehensive Evaluation (To be disclosed)

1) Evaluation on five-grade scale	S	A	B	C	D
(1) Research objective:	3	2	0	0	0
(2) Implementation of research plan:	1	4	0	0	0
(3) Research achievement:	1	4	0	0	0
(4) Future research plan:	0	5	0	0	0

S Outstanding / A Excellent / B Good / C Acceptable / D Not acceptable

2) Evaluation details (reviewer's number is different from the order of the above list)

＜Reviewer 1＞

(1) Research objective:

This is a quite ambitious research program, aiming to elucidate, control, and utilize the properties and functions originating from synergistic molecular interactions in materials with structural hierarchy. The possible outcome of this research may show strong impact in various areas.

(2) Implementation of research plan

The four research teams with focuses on molecular interaction characterization and control, biological function, and molecular integration are well organized, which consist of a broad range of experimental and theoretical researchers in areas ranging from physics, physical chemistry, synthetic organic chemistry, metalloproteins and bioengineering. Considerable attention has been paid to collaborations between teams and with researchers outside of RIKEN.

(3) Research achievement

The research achievement of each team is excellent. Collaborations between experimental and theoretical groups are very successful and highly impressive. Highlights include the development of two-dimensional fluorescence lifetime correlation spectroscopy, the discovery of pressure-induced metallic conductivity in a single-component molecular crystal and light-induced superconductivity using a photoactive electric double layer, crystal structure determination of quinol-dependent nitric oxide reductase from Geobacillus stearothermophilus, and DNA dangling-end-induced colloidal stabilization of gold nanoparticles.

(4) Future research plan

On the basis of the excellent achievements made in the last three years and towards the final goals set for this project, the future research plan is overall well conceived and should bring about further promising progress and breakthroughs. More multidisciplinary collaborations and outcomes are expected.

＜Reviewer 2＞

(1) Research objective:

The research of the project 'molecular systems research' is conducted in four research fields, led by Drs. Tahara, Kato, Shiro, and Maeda, all of whom are involved in the fundamental science and application of molecules and molecular systems. The major concept is the cross-disciplinary

investigation among physics, chemistry, biology, and engineering for highly sophisticated functional materials. They regard the fusion of various research fields as greatly important. The ‘understanding, control, and application’ of hierarchic complexity in structure, property, and function, which are not simple an integration of atoms or molecules, are the three main strategic areas for the research. They have clarified the underlying principles of hierarchic complexity by understanding the governing principles of intermolecular interactions, and have invented new functionality by controlling such interactions concertedly or by constructing specific structures, and finally are trying to apply such sophisticated exotic materials to basic devices to create new industrial fields as a future task.

Accordingly I feel the research objectives are outstanding. One thing to emphasize is that not only their concerted and cooperative interactions but also competitive activity is important for developing highly sophisticated molecular systems.

(2) Implementation of research plan:

Organization: I was very impressed by excellent research organization for the Molecular Systems Research project. The project is composed of 4 teams with 7 outstanding PIs, 3 young associate PIs, 12 talented researchers (3 of them were promoted to professor positions in a university or research institute in Japan) and postdoctoral fellows (20 foreigners) and graduate students (20 foreigners; I did not get the numbers of Japanese). The project consists of a national network of prominent scientists in excellent universities and research institutes (Kyoto Univ., Osaka Univ., Tohoku Univ., Tokyo Institute Technology, Institute for Molecular Science, and KEK).

Research size: The research group in national research institute is usually small in size especially, for graduate students. I suppose that each team in this project is also facing relatively small talented Japanese and foreign graduate students. Special program in interdisciplinary-field needs to find young graduate students and nurture them as scientific leaders for fusion research fields in next generation.

Female scientists: I was a little disappointed that this project is not able to find excellent female scientists in the higher positions.

Research meeting: For fusion research, the first step is to understand the special words and concepts used in different fields. Therefore, for the first half of the project period, a top-down program is effective to start the interdisciplinary project quickly, such as small meetings (every kind of project meeting of various sizes should be held frequently) and general meetings (every scientists in the project should attend). The success of the annual meeting, and also of the fusion research, is a consequence of these meetings. At this moment the meeting is held not so frequently.

Research period: For fusion research, after gaining an understanding of the special words and concepts for 2-3 years, the researchers have published excellent papers in the case of WPI programs. So I expect really outstanding and highly appreciated scientific papers in the fusion field to appear after such an incubation period. Therefore, I would say that a 5-year period for the fusion-field project is too short to cultivate rich product (the research period for WPI project is 10 years).

Research fund: The total budget for “competitive program for science and technology” is too small to conduct the fundamental research for fusion-field among physics, chemistry, biology, and engineering to create highly sophisticated functional molecular materials.

Accordingly, I find a mixture of excellence as well as ambitious plans that have not yet matured that has created a world-leading project for molecular sciences from materials to life.

(3) Research achievement:

I received updates on the status of their individual research programs from the team leaders. In all cases the standard of work was excellent.

Dr. Tahara’s G: This team has established world-class instruments to observe the structural dynamics of biomaterials on a μs time scale (two-dimensional fluorescence lifetime correlation spectroscopy: 2D FLCS), which has shed light on the mechanisms of bio-functions of proteins, DNA and RNA.

Dr. Kato’s G: Among the research topics in this team, the band filling control by the carrier doping into organic Mott insulator (insulator-metal-superconductor) FET system, the control of electric and magnetic properties on dual π-electronic system, and the design and preparation of new Dirac cone materials based on molecular systems are ambitious and excellent, especially the last one which is considered cutting-edge research. The organic FET of Mott insulator has a high profile in low-switching-energy transistor and ultra-high speed computers when switching at high temperature is achieved.

Dr. Shiro’s G: They constructed time-resolved IR spectroscopy to understand the detailed structure-function correlation of biologically important materials such as NO reductase. This is pioneering work.

Dr. Maeda’s G: This group has very unique principles to design, build, and develop new kinds of DNA or protein assemblies, biological logic systems, and geometrically controlled preparative methods. The way to prepare side-by-side and end-to-end assemblies by using geometrical matching is very attractive.

Total: The excellent research achievements are apparent from many interesting world-class reports published in leading journals. The leaders have a strong desire to seek applications of their findings to develop new science.

Concerning the interdisciplinary fusion research, there are several research reports within RIKEN project teams as well as with groups outside RIKEN. However, fundamental research concept of ‘collaboration’ at present and fusion research activities need more time to mature and develop coordination across teams.

Accordingly, I selected ‘A’ with the hope that this Tahara’s project indeed becomes an international hub of ‘Cross-disciplinary fusion research on molecular systems’.

(4) Future research plan:

a) Research plans within individual team: excellent

b) Research plans with other teams in this project and outside of RIKEN: need concrete plans or a project to establish an international hub of ‘Cross-disciplinary fusion research on molecular

systems'.

c) What kinds of parameters govern the specific function of molecular systems: Research subjects would be better if they would show: 1) What are the chemical, physical, or biological parameters which govern the specific function of integrative molecular systems? 2) Does the function originate from the concerted one, cooperation, competition, etc.? 3) What are the strategies to control parameter to improve or create functionality?

d) International competition: The map of world competition in each research subject is necessary. Each research subject should show perception of its strategies with respect to international competition: who and which group are their main competitors, which institutes are competitive around the world, and what are their unique advantages and disadvantages.

＜Reviewer 3＞

(1) Chief Scientist Dr. Tahei Tahara's basic idea is that material is composed of strata of assembled molecules, and he aims to treat the middle strata, that is, strata of molecular solids and biomolecular systems, and their inhomogenously mixed systems. Practically he wishes to elucidate independent and also concerted motions of molecules and resultant functions. Accordingly, Dr. Tahara determined the title of this project 'Research on Molecular System', which is defined as follows: a single kind of molecule or parts of molecules exhibiting a uniform character are assembled, and through cooperative, concerted and influential interactions of constituents with each other, the assembled system perform a unique structure, character, and function which cannot be achieved by individual components only. This is truly a cutting-edge area of chemistry meriting international recognition. Therefore, the objective of the project is noble and advanced.

(2) I think that the members of the project have been suitably selected within RIKEN. The core person working on molecular solids, Dr. Reizo Kato, is an international leader in the field of electronic properties of single-component molecular solids and their pressure control. His group has built a suitable structure of molecular assembly and succeeded in controlling its functions, such as superconductivity. The other core person, working on biomolecular systems, Dr. Yoshitsugu Shiro, is an internationally recognized leader of X-ray crystallography of heme proteins, particularly NO reducing systems. This group proposed, in addition to isolation of new enzyme systems, a unique reaction mechanism for conversion of NO to N_2O on the basis of x-ray crystallographic analysis, which is now internationally acknowledged. The two differing scientific fields are combined through a group of advanced measurements and theories, organized by Dr. Tahara. In fact, Tahara's group has developed truly new techniques for observing two-dimensional correlation fluorescence spectra to reveal dynamics of fluctuations of protein molecules in solutions and also coherent infrared sum-frequency observation to reveal structures of molecules at interfaces through molecular vibrations. The fast dynamics of proteins are also treated theoretically with molecular dynamic simulation. In the plan, the results from the three core groups of physical chemistry will be developed into optical and medical engineering for future applications by Dr. M. Maeda, the leader of the fusion team. It is not always clear at the

present stage whether this expectation will be achieved, because Dr. Maeda is a specialist in nano-particles of DNA and Dr. K. Tanaka in the fusion group is a synthetic organic chemist. The objectives of the fusion team of molecular systems and their relation to the objectives of the three core teams are not always clear to this reviewer.

The in-house members of this project seem to be sufficiently heterogeneous. I am afraid that a single leader might have difficulty understanding the achievement of individual researchers. The outside members, on the other hand, are also heterogeneous. Six leading groups of this scientific area are selected from Kyoto Univ., Tokyo Institute of Tech,, Institute for Molecular Science, Osaka Univ., Tohoku Univ. and KEK. Individual groups are active and if they are cooperated in the name of the hub institute, RIKEN, this group will be internationally acknowledged with the highest ranking. In fact, Dr. Tahara organized a large scientific research project through all Japan by using funds of MEXT, Japan, 'Soft molecular systems' to which many promising young molecular scientists participating and their presentation meeting appears to serve as the highest-ranking symposium of molecular science. This is a single example, but all the core members are working in a similar way. I had participated an international conference on Metals in Biology at RIKEN organized by Dr. Y. Shiro. Thus, Dr. Tahara and core members constitute a hub for a scientific network of material science researchers at RIKEN.

(3) I want to note that this group has organized meetings of members twice a year. One is for young researchers held every spring at an out of town venue. According to reports, about 60 to 80 persons get together and they engage in overnight poster discussions. This allows young scientists of different fields to get acquainted with each other and is expected to produce a seed for future collaboration among people with different specialties. Thus, this meeting contributes to the nurturing of young scientists. The other is a typical meeting for giving presentations summarizing each group's achievements, taking place in the autumn and winter at RIKEN. All the formal members are requested to attend and present their results for the year. Since there were about 80 participants at every meeting, this guarantees that the project facilitates mixing and discussion among scientists of different specialties.

It is good that this project has a research grant large enough to accept many posdocs (20) from other countries, including Europe, and also many graduate students (16). This serves as evidence for the fact that laboratories constituting this group actively work together internationally and are acknowledged by young scientists. The total number of such young fellows will serve as a measure for the suitable size of grant funding allotted to this project. It is only a matter of course that some members have their own collaborative laboratories outside of Japan. As a result of the high level of activity in each group, it is delightful that many young fellows who have spent some time in these laboratories are later promoted to faculty positions in various universities.

(4) Since the initial basic plan is very sound, developments of four core groups along the proposed direction will open a new scientific field in chemical science, particularly in molecular science. It is encouraging to combine researches of molecular electronic states at interface with

those of molecular assembly of Kato's group and also spectral simulation for gathering biomolecules and their reaction system with the results of Shiro's group. It is particularly interesting to elucidate magnetic purity of molecular system in terms of iron spin of a heme protein. The determination of Coulombic potential for very thin crystalline proteins by using electron microscope would become important for analysis of practical complex systems. These will serve as subjects for future challenges. It is noted that the present members are able to cover the problem areas of these future challenges and therefore this project as a whole should be continuously supported by RIKEN.

In conclusion, on the basis of the activities for three years presented, this group is expected to develop molecular science into the next level of the presumed hierarchy, opening an international frontier. Therefore, this kind of the bottom-up project research of fundamental science is a very good system and should be strongly supported in RIKEN

＜Reviewer 4＞

(1) Research objective

The objective of Molecular System Research is to elucidate, regulate and apply the structure and function of complex molecular assembly. This objective is outstanding.

(2) Implementation of research plan

The research teams are composed of physicists, chemists, engineers and biologists. In addition RIKEN scientists, scientists outside RIKEN join this project. Several interdisciplinary collaborations have been achieved.

(3) Research achievement

Research achievement of each team is excellent. However, the topics are very diverse and seem to be difficult to attract common interest and thus collaboration.

(4) Future research plan

Future plan of each team is fine. The overall research goal of this project was not clear.

＜Reviewer 5＞

1) Research objective

"The molecular systems research", that is the research on realizing highly-functional performances of molecules by using an interlocking movement and an interaction between molecules, through paying attention to hierarchy characteristics of the material reaching the compound aggregate from an isolated molecule, is quite an important subject, from the viewpoint of both basic science and future application fields. The research into elucidating the high functions of the molecular system and controlling and producing it, by concentrating the knowledge of physics, chemistry, biology and engineering, are quite important.

(2) Implementation of research plan

The study system comprised of four axes, i.e., physics about the molecular aggregate control, bio-molecular elucidation, theory and analysis to unify and understand them, the research into application of the molecules system, is thought to be effective in carrying out the molecules system research. The opportunity of creating a new development field is considered to be very high, by

cooperating and fusing the knowledge of physics, chemistry, biology and engineering, and by bringing mutual stimulation each other. The cooperation studies inside and outside RIKEN are expected to be in particular effective to enhance this project research.

At an actual research system, it is not so easy to cooperate each other, because each individual studies are in widely deferent fields. However, they realized the study system with the vigor by stimulating mutually across the field, because the individual studies carry out very high-level and the highest study in each field.

(3) Achievement of study (Research achievement)

It deserves an evaluation to achieve very high-level research results in individual studies in the physics, chemistry, biology and engineering fields concerning on the molecular systems research. The four teams created high-level results as predicted, but the following results were particularly interesting.

As for the development of optical pump-probe STM performed by analysis team, not only they enabled the luminescence measurement with molecular scale resolution, but also they succeeded in the demonstration of producing the n-type wide-bandgap semiconductor, which is useful in the application to a future high efficiency photovoltaic device. A study of the analysis of molecules provided result to engineering, and I felt the big expandability of this project to produce future application.

The research of producing gold nanoparticles with DNA by the bio-application team is also very interesting which is changing dynamically their structures. Because of the novel idea about the molecule control by DNA, the flexibility of the structural change and an impact in the application, this work is considered to be quite innovative. Particularly, the technique has an impact that a reaction (the detection) is sensitive, using a new idea (reaction only for the tip of the particle), and it has reversibility in reactions. The technique is extremely superior compared with other competitive group. This work is very meaningful in the future medical applications.

The study that controls a property of superconductor films in an organic superconductor FET device performed by the cooperation of The Institute of Molecular Science was interesting from the viewpoint of both the importance of physical phenomena on the control of the molecules crystal and application to electronics. The control of organic superconductive film by the light is also quite important from the viewpoint of production of functional active molecules and their device applications.

(4)Future research plan

Further understanding of the molecular systems is expected, by the cooperation of four area researches, to develop new phenomenon for controlling and producing inorganic or organic molecules, which can develop future applications.